

SEQUENCE LISTING

<110> DOI, Hirofumi  
 SAITO, Ken

<120> Inhibition of Nerve Cell Death by Inhibiting Degradation of SHC3, ATF6 or CREBL1 by HtrA2 and Method of Ameliorating Neurodegenerative Diseases

<130> 3190-088

<140> US Unassigned  
 <141> 2005-12-29

<150> PCT/JP2004/014378  
 <151> 2004-09-30

<150> JP P2003-342588  
 <151> 2003-09-30

<160> 37

<170> PatentIn version 3.1

<210> 1  
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 <212> DNA  
 <213> Homo sapiens

<220>  
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 <223> DNA that codes for HtrA2 precursor protein

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 tcaggaactt ctgacccccg ggcccgagtg acttatggga ccccagttct ctggggccccg 180  
 ttgtctgttg gggtcactga accccgagca tgcctgacgt ctgggacccc gggteccccg 240  
 gcacaactga ctgcggtgac ccagataacc aggacccggg aggcctcaga gaactctgga 300  
 acccggttcgc gcgcgtggct ggcggtggcg ctgggcgctg ggggggcagt gctgttgttg 360  
 ttgtggggcg ggggtcgggg tcctccggcc gtcctcgccg ccgtccctag cccgccgccc 420  
 gcttctcccc ggagtcagta caacttcata gcagatgttg tggagaagac agcacctgcc 480  
 gtggtctata tcgagatcct ggaccggcac cctttcttgg gccgcgaggt ccctatctcg 540  
 aacggctcag gattcgtggt ggctgccgat gggctcattg tcaccaacgc ccatgtggtg 600  
 gctgatcggc gcagagtccg tgtgagactg ctaagcggcg acacgtatga ggccgtggtc 660  
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 cccacgctgc ctctgggacg ctgagctgat gtcgggcaag gggagtttgt tgttgccatg 780  
 ggaagtcctt ttgactgca gaacacgata acatccggca ttgttagctc tgctcagcgt 840  
 ccagccagag acctgggact ccccaaacc aatgtggaat acattcaaac tgatgcagct 900

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attgattttg gaaactctgg aggtcccctg gttaacctgg atggggaggt gattggagtg      960
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cctgcacacc gggctggtct gcggcctggt gatgtgattt tggccattgg ggagcagatg      1260
gtacaaaatg ctgaagatgt ttatgaagct gttcgaacct aatcccagtt ggcagtgcag      1320
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<210> 2
<211> 458
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> HtrA2 precursor protein

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<400> 2

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Trp Arg Ala Leu Gly Gly Ile Arg Trp Gly Arg Arg Pro Arg Leu Thr
20           25           30

Pro Asp Leu Arg Ala Leu Leu Thr Ser Gly Thr Ser Asp Pro Arg Ala
35           40           45

Arg Val Thr Tyr Gly Thr Pro Ser Leu Trp Ala Arg Leu Ser Val Gly
50           55           60

Val Thr Glu Pro Arg Ala Cys Leu Thr Ser Gly Thr Pro Gly Pro Arg
65           70           75           80

Ala Gln Leu Thr Ala Val Thr Pro Asp Thr Arg Thr Arg Glu Ala Ser
85           90           95

Glu Asn Ser Gly Thr Arg Ser Arg Ala Trp Leu Ala Val Ala Leu Gly
100          105          110

Ala Gly Gly Ala Val Leu Leu Leu Leu Trp Gly Gly Gly Arg Gly Pro
115          120          125

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Pro Ala Val Leu Ala Ala Val Pro Ser Pro Pro Pro Ala Ser Pro Arg  
 130 135 140

Ser Gln Tyr Asn Phe Ile Ala Asp Val Val Glu Lys Thr Ala Pro Ala  
 145 150 155 160

Val Val Tyr Ile Glu Ile Leu Asp Arg His Pro Phe Leu Gly Arg Glu  
 165 170 175

Val Pro Ile Ser Asn Gly Ser Gly Phe Val Val Ala Ala Asp Gly Leu  
 180 185 190

Ile Val Thr Asn Ala His Val Val Ala Asp Arg Arg Arg Val Arg Val  
 195 200 205

Arg Leu Leu Ser Gly Asp Thr Tyr Glu Ala Val Val Thr Ala Val Asp  
 210 215 220

Pro Val Ala Asp Ile Ala Thr Leu Arg Ile Gln Thr Lys Glu Pro Leu  
 225 230 235 240

Pro Thr Leu Pro Leu Gly Arg Ser Ala Asp Val Arg Gln Gly Glu Phe  
 245 250 255

Val Val Ala Met Gly Ser Pro Phe Ala Leu Gln Asn Thr Ile Thr Ser  
 260 265 270

Gly Ile Val Ser Ser Ala Gln Arg Pro Ala Arg Asp Leu Gly Leu Pro  
 275 280 285

Gln Thr Asn Val Glu Tyr Ile Gln Thr Asp Ala Ala Ile Asp Phe Gly  
 290 295 300

Asn Ser Gly Gly Pro Leu Val Asn Leu Asp Gly Glu Val Ile Gly Val  
 305 310 315 320

Asn Thr Met Lys Val Thr Ala Gly Ile Ser Phe Ala Ile Pro Ser Asp  
 325 330 335

Arg Leu Arg Glu Phe Leu His Arg Gly Glu Lys Lys Asn Ser Ser Ser  
 340 345 350

Gly Ile Ser Gly Ser Gln Arg Arg Tyr Ile Gly Val Met Met Leu Thr  
 355 360 365

Leu Ser Pro Ser Ile Leu Ala Glu Leu Gln Leu Arg Glu Pro Ser Phe  
 370 375 380

Pro Asp Val Gln His Gly Val Leu Ile His Lys Val Ile Leu Gly Ser  
385 390 395 400

Pro Ala His Arg Ala Gly Leu Arg Pro Gly Asp Val Ile Leu Ala Ile  
405 410 415

Gly Glu Gln Met Val Gln Asn Ala Glu Asp Val Tyr Glu Ala Val Arg  
420 425 430

Thr Gln Ser Gln Leu Ala Val Gln Ile Arg Arg Gly Arg Glu Thr Leu  
435 440 445

Thr Leu Tyr Val Thr Pro Glu Val Thr Glu  
450 455

<210> 3  
<211> 981  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<223> DNA that codes for mature HtrA2

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ttgggccgag aggtccctat ctggaacggc tcaggattcg tgggtggctgc cgatgggctc 180  
attgtcacca acgcccattg ggtggctgat cggcgagag tccgtgtgag actgctaagc 240  
ggcgacacgt atgaggccgt ggtcacagct gtggatcccg tggcagacat cgcaacgctg 300  
aggattcaga ctaaggagcc tctccccacg ctgcctctgg gacgctcagc tgatgtcccg 360  
caaggggagt ttgttgttgc catgggaagt ccctttgcac tgcagaacac gatcacatcc 420  
ggcattgtta gctctgtcga gcgtccagcc agagacctgg gactccccca aaccaatgtg 480  
gaatacatto aaactgatgc agctattgat tttggaaact ctggaggtcc cctgggttaac 540  
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ggaatcagtg ggtcccagcg gcgctacatt ggggtgatga tgctgaccct gagtcccagc 720  
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atccataaag tcattctggg ctcccctgca caccgggctg gtctgcggcc tggatgatgtg 840  
atcttggcca ttggggagca gatggtacaa aatgctgaag atgtttatga agctgttoga 900  
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accctgagg tcacagaatg a

981

<210> 4  
<211> 326  
<212> PRT  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<223> mature HtrA2

<400> 4

Met Ala Val Pro Ser Pro Pro Pro Ala Ser Pro Arg Ser Gln Tyr Asn  
1 5 10 15

Phe Ile Ala Asp Val Val Glu Lys Thr Ala Pro Ala Val Val Tyr Ile  
20 25 30

Glu Ile Leu Asp Arg His Pro Phe Leu Gly Arg Glu Val Pro Ile Ser  
35 40 45

Asn Gly Ser Gly Phe Val Val Ala Ala Asp Gly Leu Ile Val Thr Asn  
50 55 60

Ala His Val Val Ala Asp Arg Arg Arg Val Arg Val Arg Leu Leu Ser  
65 70 75 80

Gly Asp Thr Tyr Glu Ala Val Val Thr Ala Val Asp Pro Val Ala Asp  
85 90 95

Ile Ala Thr Leu Arg Ile Gln Thr Lys Glu Pro Leu Pro Thr Leu Pro  
100 105 110

Leu Gly Arg Ser Ala Asp Val Arg Gln Gly Glu Phe Val Val Ala Met  
115 120 125

Gly Ser Pro Phe Ala Leu Gln Asn Thr Ile Thr Ser Gly Ile Val Ser  
130 135 140

Ser Ala Gln Arg Pro Ala Arg Asp Leu Gly Leu Pro Gln Thr Asn Val  
145 150 155 160

Glu Tyr Ile Gln Thr Asp Ala Ala Ile Asp Phe Gly Asn Ser Gly Gly  
165 170 175

Pro Leu Val Asn Leu Asp Gly Glu Val Ile Gly Val Asn Thr Met Lys  
180 185 190

Val Thr Ala Gly Ile Ser Phe Ala Ile Pro Ser Asp Arg Leu Arg Glu  
195 200 205

Phe Leu His Arg Gly Glu Lys Lys Asn Ser Ser Ser Gly Ile Ser Gly  
210 215 220

Ser Gln Arg Arg Tyr Ile Gly Val Met Met Leu Thr Leu Ser Pro Ser  
225 230 235 240

Ile Leu Ala Glu Leu Gln Leu Arg Glu Pro Ser Phe Pro Asp Val Gln  
245 250 255

His Gly Val Leu Ile His Lys Val Ile Leu Gly Ser Pro Ala His Arg  
260 265 270

Ala Gly Leu Arg Pro Gly Asp Val Ile Leu Ala Ile Gly Glu Gln Met  
275 280 285

Val Gln Asn Ala Glu Asp Val Tyr Glu Ala Val Arg Thr Gln Ser Gln  
290 295 300

Leu Ala Val Gln Ile Arg Arg Gly Arg Glu Thr Leu Thr Leu Tyr Val  
305 310 315 320

Thr Pro Glu Val Thr Glu  
325

<210> 5  
<211> 981  
<212> DNA  
<213> Artificial

<220>  
<223> Polynucleotide consisting of the same base sequence of SEQ ID NO:  
3 wherein the nucleotide of position 520 is g

<220>  
<221> misc\_feature  
<223> DNA that codes for mature HtrA2(S306A)

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ttgggccgag aggtccctat ctggaacggc tcaggattcg tgggtggctgc cgatgggctc 180  
attgtcacca acgcccattg ggtggctgat cggcgagag tccgtgtgag actgctaagc 240  
ggcgacacgt atgaggccgt ggtcacagct gtggatcccg tggcagacat cgcaacgctg 300  
aggattcaga ctaaggagcc tctccccacg ctgcctctgg gacgctcagc tgatgtccgg 360

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caaggggagtt ttgttggtgc catgggaagt ccctttgcac tgcagaacac gatcacatcc 420
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gaatacattc aaactgatgc agctattgat ttggaaacg ctggaggtcc cctggttaac 540
ctggatgggg aggtgattgg agtgaacacc atgaaggatca cagctggaat ctcctttgcc 600
atcccttctg atcgtcttcg agagtttctg catcgtgggg aaaagaagaa ttcctcctcc 660
ggaatcagtg ggtcccagcg gcgctacatt ggggtgatga tgctgaccct gagtcccagc 720
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atccataaag tcatactggg ctcccctgca caccgggctg gtctgcggcc tggatgatgtg 840
attttgcca ttggggagca gatggtacaa aatgctgaag atgtttatga agctgttcga 900
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<210> 6
<211> 326
<212> PRT
<213> Artificial

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<220>
<223> Polypeptide consisting of the same amino acid sequence of SEQ ID
      NO:4 wherein the 174th amino acid residue is substituted by Ala

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<220>
<221> misc_feature
<223> mature HtrA2 (S306A)

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<400> 6

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Met Ala Val Pro Ser Pro Pro Pro Ala Ser Pro Arg Ser Gln Tyr Asn
1          5          10          15

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Phe Ile Ala Asp Val Val Glu Lys Thr Ala Pro Ala Val Val Tyr Ile
20          25          30

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Glu Ile Leu Asp Arg His Pro Phe Leu Gly Arg Glu Val Pro Ile Ser
35          40          45

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Asn Gly Ser Gly Phe Val Val Ala Ala Asp Gly Leu Ile Val Thr Asn
50          55          60

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Ala His Val Val Ala Asp Arg Arg Arg Val Arg Val Arg Leu Leu Ser
65          70          75          80

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Gly Asp Thr Tyr Glu Ala Val Val Thr Ala Val Asp Pro Val Ala Asp
85          90          95

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Ile Ala Thr Leu Arg Ile Gln Thr Lys Glu Pro Leu Pro Thr Leu Pro  
100 105 110

Leu Gly Arg Ser Ala Asp Val Arg Gln Gly Glu Phe Val Val Ala Met  
115 120 125

Gly Ser Pro Phe Ala Leu Gln Asn Thr Ile Thr Ser Gly Ile Val Ser  
130 135 140

Ser Ala Gln Arg Pro Ala Arg Asp Leu Gly Leu Pro Gln Thr Asn Val  
145 150 155 160

Glu Tyr Ile Gln Thr Asp Ala Ala Ile Asp Phe Gly Asn Ala Gly Gly  
165 170 175

Pro Leu Val Asn Leu Asp Gly Glu Val Ile Gly Val Asn Thr Met Lys  
180 185 190

Val Thr Ala Gly Ile Ser Phe Ala Ile Pro Ser Asp Arg Leu Arg Glu  
195 200 205

Phe Leu His Arg Gly Glu Lys Lys Asn Ser Ser Ser Gly Ile Ser Gly  
210 215 220

Ser Gln Arg Arg Tyr Ile Gly Val Met Met Leu Thr Leu Ser Pro Ser  
225 230 235 240

Ile Leu Ala Glu Leu Gln Leu Arg Glu Pro Ser Phe Pro Asp Val Gln  
245 250 255

His Gly Val Leu Ile His Lys Val Ile Leu Gly Ser Pro Ala His Arg  
260 265 270

Ala Gly Leu Arg Pro Gly Asp Val Ile Leu Ala Ile Gly Glu Gln Met  
275 280 285

Val Gln Asn Ala Glu Asp Val Tyr Glu Ala Val Arg Thr Gln Ser Gln  
290 295 300

Leu Ala Val Gln Ile Arg Arg Gly Arg Glu Thr Leu Thr Leu Tyr Val  
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Thr Pro Glu Val Thr Glu  
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<210> 7  
<211> 969



<212> DNA  
<213> Artificial

<220>  
<223> Polynucleotide consisting of the same base sequence of SEQ ID NO: 3 wherein the nucleotides of position 4-15 are deleted

<220>  
<221> misc\_feature  
<223> DNA that codes for mature HtrA2(delta AVPS)

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gtccctatct cgaacggctc aggattcgtg gtggctgccc atgggctcat tgtcaccaac 180  
gcccattgtg tggctgatcg gcgcagagtc cgtgtgagac tgctaagcgg cgacacgtat 240  
gaggccgtgg tcacagctgt ggatcccgtg gcagacatcg caacgctgag gattcagact 300  
aaggagcctc tccccacgct gcctctggga cgctcagctg atgtccggca aggggagttt 360  
gttgttgcca tgggaagtcc ctttgactg cagaacacga tcacatccgg cattgttagc 420  
tctgctcagc gtccagccag agacctggga ctcccccaaa ccaatgtgga atacattcaa 480  
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cgtcttcgag agtttctgca tcgtggggaa aagaagaatt cctcctccgg aatcagtgga 660  
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acagaatga 969

<210> 8  
<211> 322  
<212> PRT  
<213> Artificial

<220>  
<223> Polypeptide consisting of the same amino acid sequence of SEQ ID NO:4 wherein the amino acid residues from the 2nd to the 5th are deleted

<220>  
<221> misc\_feature  
<223> mature HtrA2(delta AVPS)

<400> 8

Met Pro Pro Pro Ala Ser Pro Arg Ser Gln Tyr Asn Phe Ile Ala Asp  
1 5 10 15

Val Val Glu Lys Thr Ala Pro Ala Val Val Tyr Ile Glu Ile Leu Asp  
20 25 30

Arg His Pro Phe Leu Gly Arg Glu Val Pro Ile Ser Asn Gly Ser Gly  
35 40 45

Phe Val Val Ala Ala Asp Gly Leu Ile Val Thr Asn Ala His Val Val  
50 55 60

Ala Asp Arg Arg Arg Val Arg Val Arg Leu Leu Ser Gly Asp Thr Tyr  
65 70 75 80

Glu Ala Val Val Thr Ala Val Asp Pro Val Ala Asp Ile Ala Thr Leu  
85 90 95

Arg Ile Gln Thr Lys Glu Pro Leu Pro Thr Leu Pro Leu Gly Arg Ser  
100 105 110

Ala Asp Val Arg Gln Gly Glu Phe Val Val Ala Met Gly Ser Pro Phe  
115 120 125

Ala Leu Gln Asn Thr Ile Thr Ser Gly Ile Val Ser Ser Ala Gln Arg  
130 135 140

Pro Ala Arg Asp Leu Gly Leu Pro Gln Thr Asn Val Glu Tyr Ile Gln  
145 150 155 160

Thr Asp Ala Ala Ile Asp Phe Gly Asn Ser Gly Gly Pro Leu Val Asn  
165 170 175

Leu Asp Gly Glu Val Ile Gly Val Asn Thr Met Lys Val Thr Ala Gly  
180 185 190

Ile Ser Phe Ala Ile Pro Ser Asp Arg Leu Arg Glu Phe Leu His Arg  
195 200 205

Gly Glu Lys Lys Asn Ser Ser Ser Gly Ile Ser Gly Ser Gln Arg Arg  
210 215 220

Tyr Ile Gly Val Met Met Leu Thr Leu Ser Pro Ser Ile Leu Ala Glu  
225 230 235 240

Leu Gln Leu Arg Glu Pro Ser Phe Pro Asp Val Gln His Gly Val Leu

245

250

255

Ile His Lys Val Ile Leu Gly Ser Pro Ala His Arg Ala Gly Leu Arg  
 260 265 270

Pro Gly Asp Val Ile Leu Ala Ile Gly Glu Gln Met Val Gln Asn Ala  
 275 280 285

Glu Asp Val Tyr Glu Ala Val Arg Thr Gln Ser Gln Leu Ala Val Gln  
 290 295 300

Ile Arg Arg Gly Arg Glu Thr Leu Thr Leu Tyr Val Thr Pro Glu Val  
 305 310 315 320

Thr Glu

<210> 9  
 <211> 981  
 <212> DNA  
 <213> Artificial

<220>  
 <223> Polynucleotide consisting of the same base sequence of SEQ ID NO:  
 3 wherein the nucleotide of position 5 is g

<220>  
 <221> misc\_feature  
 <223> DNA that codes for mature HtrA2 (GVPS)

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 ttggggccgag aggtccctat ctggaacggc tcaggattcg tgggtggctgc cgatgggctc 180  
 attgtcacca acgcccattg ggtggctgat cggcgagag tccgtgtgag actgctaagc 240  
 ggcgacacgt atgaggccgt ggtcacagct gtggatcccg tggcagacat cgcaacgctg 300  
 aggattcaga ctaaggagcc tctccccacg ctgcctctgg gacgctcagc tgatgtccgg 360  
 caaggggagt ttgttgttgc catgggaagt ccctttgcac tgcagaacac gatcacatcc 420  
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 acccctgagg tcacagaatg a 981

<210> 10  
 <211> 326  
 <212> PRT  
 <213> Artificial

<220>  
 <223> Polypeptide consisting of the same amino acid sequence of SEQ ID NO:4 wherein the 2nd amino acid residue is substituted by Gly

<220>  
 <221> misc\_feature  
 <223> mature HtrA2 (GVPS)

<400> 10

Met Gly Val Pro Ser Pro Pro Pro Ala Ser Pro Arg Ser Gln Tyr Asn  
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Phe Ile Ala Asp Val Val Glu Lys Thr Ala Pro Ala Val Val Tyr Ile  
 20 25 30

Glu Ile Leu Asp Arg His Pro Phe Leu Gly Arg Glu Val Pro Ile Ser  
 35 40 45

Asn Gly Ser Gly Phe Val Val Ala Ala Asp Gly Leu Ile Val Thr Asn  
 50 55 60

Ala His Val Val Ala Asp Arg Arg Arg Val Arg Val Arg Leu Leu Ser  
 65 70 75 80

Gly Asp Thr Tyr Glu Ala Val Val Thr Ala Val Asp Pro Val Ala Asp  
 85 90 95

Ile Ala Thr Leu Arg Ile Gln Thr Lys Glu Pro Leu Pro Thr Leu Pro  
 100 105 110

Leu Gly Arg Ser Ala Asp Val Arg Gln Gly Glu Phe Val Val Ala Met  
 115 120 125

Gly Ser Pro Phe Ala Leu Gln Asn Thr Ile Thr Ser Gly Ile Val Ser  
 130 135 140

Ser Ala Gln Arg Pro Ala Arg Asp Leu Gly Leu Pro Gln Thr Asn Val



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acagcacctg ccgtggtcta tatcgagatc ctggaccggc accctttctt gggccgcgag      120
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gcccattgtg tggtgatcg gcgcagagtc cgtgtgagac tgctaagcgg cgacacgtat      240
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ctacagcttc gagaaccaag ctttcccgat gttcagcatg gtgtactcat ccataaagtc      780
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<210> 12
<211> 322
<212> PRT
<213> Artificial

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<220>
<223> Polypeptide consisting of the same amino acid sequence of SEQ ID
      NO:6 wherein the amino acid residues from the 2nd to the 5th are
      deleted

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<220>
<221> misc_feature
<223> mature HtrA2(S306A, delta AVPS)

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<400> 12

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Met Pro Pro Pro Ala Ser Pro Arg Ser Gln Tyr Asn Phe Ile Ala Asp
1           5           10           15

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Val Val Glu Lys Thr Ala Pro Ala Val Val Tyr Ile Glu Ile Leu Asp
          20           25           30

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```

Arg His Pro Phe Leu Gly Arg Glu Val Pro Ile Ser Asn Gly Ser Gly
          35           40           45

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Phe Val Val Ala Ala Asp Gly Leu Ile Val Thr Asn Ala His Val Val  
 50 55 60

Ala Asp Arg Arg Arg Val Arg Val Arg Leu Leu Ser Gly Asp Thr Tyr  
 65 70 75 80

Glu Ala Val Val Thr Ala Val Asp Pro Val Ala Asp Ile Ala Thr Leu  
 85 90 95

Arg Ile Gln Thr Lys Glu Pro Leu Pro Thr Leu Pro Leu Gly Arg Ser  
 100 105 110

Ala Asp Val Arg Gln Gly Glu Phe Val Val Ala Met Gly Ser Pro Phe  
 115 120 125

Ala Leu Gln Asn Thr Ile Thr Ser Gly Ile Val Ser Ser Ala Gln Arg  
 130 135 140

Pro Ala Arg Asp Leu Gly Leu Pro Gln Thr Asn Val Glu Tyr Ile Gln  
 145 150 155 160

Thr Asp Ala Ala Ile Asp Phe Gly Asn Ala Gly Gly Pro Leu Val Asn  
 165 170 175

Leu Asp Gly Glu Val Ile Gly Val Asn Thr Met Lys Val Thr Ala Gly  
 180 185 190

Ile Ser Phe Ala Ile Pro Ser Asp Arg Leu Arg Glu Phe Leu His Arg  
 195 200 205

Gly Glu Lys Lys Asn Ser Ser Ser Gly Ile Ser Gly Ser Gln Arg Arg  
 210 215 220

Tyr Ile Gly Val Met Met Leu Thr Leu Ser Pro Ser Ile Leu Ala Glu  
 225 230 235 240

Leu Gln Leu Arg Glu Pro Ser Phe Pro Asp Val Gln His Gly Val Leu  
 245 250 255

Ile His Lys Val Ile Leu Gly Ser Pro Ala His Arg Ala Gly Leu Arg  
 260 265 270

Pro Gly Asp Val Ile Leu Ala Ile Gly Glu Gln Met Val Gln Asn Ala  
 275 280 285

Glu Asp Val Tyr Glu Ala Val Arg Thr Gln Ser Gln Leu Ala Val Gln  
 290 295 300

Ile Arg Arg Gly Arg Glu Thr Leu Thr Leu Tyr Val Thr Pro Glu Val  
 305 310 315 320

Thr Glu

<210> 13  
 <211> 981  
 <212> DNA  
 <213> Artificial

<220>  
 <223> Polynucleotide consisting of the same base sequence of SEQ ID NO:  
 5 wherein the nucleotide of position 5 is g

<220>  
 <221> misc\_feature  
 <223> DNA that codes for mature HtrA2(S306A, GVPS)

<400> 13  
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 gtggtggaga agacagcacc tgccgtggtc tatatcgaga tcctggaccg gcaccctttc 120  
 ttgggccgag aggtccctat ctcgaaacggc tcaggattcg tggtaggctgc cgatgggctc 180  
 attgtcacca acgcccattg ggtggctgat cggcgacagag tccgtgtgag actgctaagc 240  
 ggcgacacgt atgaggccgt ggtcacagct gtggatcccg tggcagacat cgcaacgctg 300  
 aggattcaga ctaaggagcc tctccccacg ctgcctctgg gacgctcagc tgatgtccgg 360  
 caaggggagt ttgtttgttc catgggaagt ccctttgcac tgcagaacac gatcacatcc 420  
 ggcatgttta gctctgtctc gcgtccagcc agagacctgg gactccccca aaccaatgtg 480  
 gaatacatte aaactgatgc agctattgat tttggaaacg ctggaggtcc cctgggttaac 540  
 ctggatgggg aggtgattgg agtgaacacc atgaaggatc cagctggaat ctcccttgcc 600  
 atcccttctg atcgtcttcg agagtttctg catcgtgggg aaaagaagaa ttcctcctcc 660  
 ggaatcagtg ggtcccagcg gcgctacatt ggggtgatga tgctgaccct gagtcccagc 720  
 atccttgctg aactacagct tcgagaacca agctttcccg atgttcagca tgggtgtactc 780  
 atccataaag tcctcctggg ctcccctgca caccgggctg gtctgcggcc tggatgatgtg 840  
 attttgcca ttggggagca gatggtacaa aatgctgaag atgtttatga agctgttcga 900  
 acccaatccc agttggcagt gcagatccgg cggggacgag aaacactgac cttatatgtg 960  
 acccctgagg tcacagaatg a 981

<210> 14  
 <211> 326  
 <212> PRT  
 <213> Artificial



<220>

<223> Polypeptide consisting of the same amino acid sequence of SEQ ID NO:6 wherein the 2nd amino acid residue is substituted by Gly

<220>

<221> misc\_feature

<223> mature HtrA2(S306A, GVPS)

<400> 14

Met Gly Val Pro Ser Pro Pro Pro Ala Ser Pro Arg Ser Gln Tyr Asn  
1 5 10 15

Phe Ile Ala Asp Val Val Glu Lys Thr Ala Pro Ala Val Val Tyr Ile  
20 25 30

Glu Ile Leu Asp Arg His Pro Phe Leu Gly Arg Glu Val Pro Ile Ser  
35 40 45

Asn Gly Ser Gly Phe Val Val Ala Ala Asp Gly Leu Ile Val Thr Asn  
50 55 60

Ala His Val Val Ala Asp Arg Arg Arg Val Arg Val Arg Leu Leu Ser  
65 70 75 80

Gly Asp Thr Tyr Glu Ala Val Val Thr Ala Val Asp Pro Val Ala Asp  
85 90 95

Ile Ala Thr Leu Arg Ile Gln Thr Lys Glu Pro Leu Pro Thr Leu Pro  
100 105 110

Leu Gly Arg Ser Ala Asp Val Arg Gln Gly Glu Phe Val Val Ala Met  
115 120 125

Gly Ser Pro Phe Ala Leu Gln Asn Thr Ile Thr Ser Gly Ile Val Ser  
130 135 140

Ser Ala Gln Arg Pro Ala Arg Asp Leu Gly Leu Pro Gln Thr Asn Val  
145 150 155 160

Glu Tyr Ile Gln Thr Asp Ala Ala Ile Asp Phe Gly Asn Ala Gly Gly  
165 170 175

Pro Leu Val Asn Leu Asp Gly Glu Val Ile Gly Val Asn Thr Met Lys  
180 185 190

Val Thr Ala Gly Ile Ser Phe Ala Ile Pro Ser Asp Arg Leu Arg Glu  
195 200 205

Phe Leu His Arg Gly Glu Lys Lys Asn Ser Ser Ser Gly Ile Ser Gly  
 210 215 220  
 Ser Gln Arg Arg Tyr Ile Gly Val Met Met Leu Thr Leu Ser Pro Ser  
 225 230 235 240  
 Ile Leu Ala Glu Leu Gln Leu Arg Glu Pro Ser Phe Pro Asp Val Gln  
 245 250 255  
 His Gly Val Leu Ile His Lys Val Ile Leu Gly Ser Pro Ala His Arg  
 260 265 270  
 Ala Gly Leu Arg Pro Gly Asp Val Ile Leu Ala Ile Gly Glu Gln Met  
 275 280 285  
 Val Gln Asn Ala Glu Asp Val Tyr Glu Ala Val Arg Thr Gln Ser Gln  
 290 295 300  
 Leu Ala Val Gln Ile Arg Arg Gly Arg Glu Thr Leu Thr Leu Tyr Val  
 305 310 315 320  
 Thr Pro Glu Val Thr Glu  
 325

<210> 15  
 <211> 1785  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> DNA that codes for SHC3

<400> 15  
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 cttctccaca gcctgtcggg gagcggcggc ggaggcaagg ttctggcggc gcgcgcgacc 120  
 ccggcggcgg ctccctactt ggtgtccggc gaggcgctgc gcaaggcgcc cgacgatggg 180  
 cccggcagcc tgggccacct gctccacaag gtgtcccacc tgaaactctc cagctcgggc 240  
 ctccgcggcc tgtcgtcggc cgcccgggag cgggcggggc cgcggtcttc gggcagctgc 300  
 agcgcgcca gcctggccgc ccgggacggc agtgcgccct cggcgccccg cgccccggcc 360  
 atgagcgccg ccaggaaggg ccggcccggc gacgagccgc tgcccaggcc ccctcggggg 420  
 gcgcgcacg ccagcgacca ggtgctgggg ccgggagtca cctacgtggt caagtacttg 480  
 ggggtgcattg aagttctgcg ctcaatgagg tctcttgact tcagtacaag aacacaaatt 540  
 accagggaag ccatcagccg cgtctgtgaa gctgtgcctg gtgcgaaggg agccttcaag 600

aagagaaagc ctccaagcaa aatgctgtcc agcatcttgg gaaagagcaa cctccagttt 660  
gcgggaatga gcatctctct gaccatctcc acggccagtc tgaacctgcg aactccggac 720  
tccaaacaga tcatagcgaa tcaccacatg cgggtccatct ccttcgcctc tgggggagac 780  
ccggacacaa ctgactatgt tgcataatgt gctaaggacc ctgttaatcg cagagcttgt 840  
cacatttttg aatgctgtga tgggctggcc caggatgtca tcggctccat cggacaagcc 900  
tttgagctcc ggtttaagca atatttacag tgtcctacca agattcccgc tctccatgat 960  
cgaatgcaga gtctggatga gccatggacg gaagaggagg gagatggctc agaccaccca 1020  
tactacaaca gcatcccaag caagatgcct cctccagggg gctttcttga tactagactg 1080  
aaaccacagc cccatgctcc tgacacagcc cagtttgcag gaaaagagca gacttattac 1140  
cagggaagac acttaggaga cacttttggc gaagactggc agcaaacacc tttaaggcaa 1200  
gggtcctcgg acatctacag cacgccagaa gggaaactgc acgtggcccc cacgggagaa 1260  
gcacccacct acgtcaacac tcagcagatc ccaccacagg cctggccggc tgcggtcagc 1320  
agtgtctgaga gcagcccaag gaaagacctc tttgacatga aaccttttga agatgtcttc 1380  
aagaaccagc ccttggggcc cgtgttaagc aaggcagcct ccgtggagtg catcagccct 1440  
gtgtcaccta gagccccaga tgccaagatg ctggaggaac tgcaagccga gacttggtac 1500  
caaggagaga tgagcaggaa ggaggcagag gggctgctgg agaaagacgg agacttcctg 1560  
gtcaggaaga gcaccaccaa cccgggctcc tttgtcctca cgggcatgca caatggccag 1620  
gccaaagcacc tgctgctcgt ggaccacagaa ggacagatcc ggacaaagga cagagtcttt 1680  
gacagtatca gccacctcat caaccaccac ctagaaagca gcctgcccac tgtctctgca 1740  
gggagtgagc tgtgtctcca gcagccagtg gagaggaagc agtga 1785

<210> 16  
<211> 594  
<212> PRT  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<223> SHC3

<400> 16

Met Leu Pro Arg Thr Lys Tyr Asn Arg Phe Arg Asn Asp Ser Val Thr  
1 5 10 15

Ser Val Asp Asp Leu Leu His Ser Leu Ser Val Ser Gly Gly Gly Gly  
20 25 30

Lys Val Ser Ala Ala Arg Ala Thr Pro Ala Ala Ala Pro Tyr Leu Val

Ser Gly Glu Ala Leu Arg Lys Ala Pro Asp Asp Gly Pro Gly Ser Leu  
50 55 60

Gly His Leu Leu His Lys Val Ser His Leu Lys Leu Ser Ser Ser Gly  
65 70 75 80

Leu Arg Gly Leu Ser Ser Ala Ala Arg Glu Arg Ala Gly Ala Arg Leu  
85 90 95

Ser Gly Ser Cys Ser Ala Pro Ser Leu Ala Ala Pro Asp Gly Ser Ala  
100 105 110

Pro Ser Ala Pro Arg Ala Pro Ala Met Ser Ala Ala Arg Lys Gly Arg  
115 120 125

Pro Gly Asp Glu Pro Leu Pro Arg Pro Pro Arg Gly Ala Pro His Ala  
130 135 140

Ser Asp Gln Val Leu Gly Pro Gly Val Thr Tyr Val Val Lys Tyr Leu  
145 150 155 160

Gly Cys Ile Glu Val Leu Arg Ser Met Arg Ser Leu Asp Phe Ser Thr  
165 170 175

Arg Thr Gln Ile Thr Arg Glu Ala Ile Ser Arg Val Cys Glu Ala Val  
180 185 190

Pro Gly Ala Lys Gly Ala Phe Lys Lys Arg Lys Pro Pro Ser Lys Met  
195 200 205

Leu Ser Ser Ile Leu Gly Lys Ser Asn Leu Gln Phe Ala Gly Met Ser  
210 215 220

Ile Ser Leu Thr Ile Ser Thr Ala Ser Leu Asn Leu Arg Thr Pro Asp  
225 230 235 240

Ser Lys Gln Ile Ile Ala Asn His His Met Arg Ser Ile Ser Phe Ala  
245 250 255

Ser Gly Gly Asp Pro Asp Thr Thr Asp Tyr Val Ala Tyr Val Ala Lys  
260 265 270

Asp Pro Val Asn Arg Arg Ala Cys His Ile Leu Glu Cys Cys Asp Gly  
275 280 285

Leu Ala Gln Asp Val Ile Gly Ser Ile Gly Gln Ala Phe Glu Leu Arg  
 290 295 300

Phe Lys Gln Tyr Leu Gln Cys Pro Thr Lys Ile Pro Ala Leu His Asp  
 305 310 315 320

Arg Met Gln Ser Leu Asp Glu Pro Trp Thr Glu Glu Glu Gly Asp Gly  
 325 330 335

Ser Asp His Pro Tyr Tyr Asn Ser Ile Pro Ser Lys Met Pro Pro Pro  
 340 345 350

Gly Gly Phe Leu Asp Thr Arg Leu Lys Pro Arg Pro His Ala Pro Asp  
 355 360 365

Thr Ala Gln Phe Ala Gly Lys Glu Gln Thr Tyr Tyr Gln Gly Arg His  
 370 375 380

Leu Gly Asp Thr Phe Gly Glu Asp Trp Gln Gln Thr Pro Leu Arg Gln  
 385 390 395 400

Gly Ser Ser Asp Ile Tyr Ser Thr Pro Glu Gly Lys Leu His Val Ala  
 405 410 415

Pro Thr Gly Glu Ala Pro Thr Tyr Val Asn Thr Gln Gln Ile Pro Pro  
 420 425 430

Gln Ala Trp Pro Ala Ala Val Ser Ser Ala Glu Ser Ser Pro Arg Lys  
 435 440 445

Asp Leu Phe Asp Met Lys Pro Phe Glu Asp Ala Leu Lys Asn Gln Pro  
 450 455 460

Leu Gly Pro Val Leu Ser Lys Ala Ala Ser Val Glu Cys Ile Ser Pro  
 465 470 475 480

Val Ser Pro Arg Ala Pro Asp Ala Lys Met Leu Glu Glu Leu Gln Ala  
 485 490 495

Glu Thr Trp Tyr Gln Gly Glu Met Ser Arg Lys Glu Ala Glu Gly Leu  
 500 505 510

Leu Glu Lys Asp Gly Asp Phe Leu Val Arg Lys Ser Thr Thr Asn Pro  
 515 520 525

Gly Ser Phe Val Leu Thr Gly Met His Asn Gly Gln Ala Lys His Leu  
 530 535 540

Leu Leu Val Asp Pro Glu Gly Thr Ile Arg Thr Lys Asp Arg Val Phe  
 545 550 555 560

Asp Ser Ile Ser His Leu Ile Asn His His Leu Glu Ser Ser Leu Pro  
 565 570 575

Ile Val Ser Ala Gly Ser Glu Leu Cys Leu Gln Gln Pro Val Glu Arg  
 580 585 590

Lys Gln

<210> 17  
 <211> 2112  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> DNA that codes for CREBL1

<400> 17  
 atggcggagc tgatgctgct cagcgagatt gctgaccoga cgcgtttctt caccgacaac 60  
 ctgcttagcc cggaggactg gggctcgcag aacagcacct tgtattcttg cctagatgaa 120  
 gtggccgagg agcagacgca gctcttccgt tgcccgagc aggatgtccc gtttgacggc 180  
 agctccctgg acgtggggat ggatgtcagc ccctctgagc ccccatggga actcctgccg 240  
 atcttcccag atcttcaggt gaagtctgag ccatcttccc cctgctcttc ctctccctc 300  
 agctccgagt catcgctct ctccacagag ccatccagcg aggctcttg ggtaggggag 360  
 gtgctccatg tgaagacaga gtccttgga ccccaactgt gtctcctgg agatgaccca 420  
 acatctcat ttgaaaccgt ccagatcaat gttatcccca cctctgatga ttcctcagat 480  
 gtccagacca agatagaacc tgtctctcca tgttcttccg tcaactctga ggcctccctg 540  
 ctctcagccg actcctccag ccaggctttt ataggagagg aggtcctgga agtgaagaca 600  
 gagtccctgt ccccttcagg atgcctcctg tgggatgtcc cagccccctc acttgagct 660  
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 aagccgccac tgcagcccaa acctgtagt ctaaccactg tccaatgcc atccagagct 780  
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 gtggatgcaa agctgctgaa gcggcagcag cgaatgatca agaaccggga gtcagcctgc 1020  
 cagtcccga gaaagaagaa agagtatctg cagggactgg aggctcggct gcaagcagta 1080

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ctggctgaca accagcagct ccgccgagag aatgctgccc tccggcggcg gctggaggcc 1140
ctgctggctg aaaacagcga gctcaagtta gggctctggaa acaggaaggt ggtctgcatc 1200
atggtcttcc ttctcttcat tgccttcaac tttggacctg tcagcatcag tgagcctcct 1260
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tgccggcact tcaaccgcac tgagtcctg aggcttgctg acgagttgag tggctgggtc 1560
cagcgccacc agagaggccg gaggaagatc cctcagaggg cccaggagag acagaagtct 1620
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gagatgatgc agatcgagtg tgaggtcatg gacaccaggg tgattcacat caagacctcc 1980
acagtgcccc cctcgctccg aaaacagcca tccccaaccc caggcaatgc cacaggtggc 2040
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aatcatccct aa 2112

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<210> 18
<211> 703
<212> PRT
<213> Homo sapiens

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<220>
<221> misc_feature
<223> CREBL1

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<400> 18

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Met Ala Glu Leu Met Leu Leu Ser Glu Ile Ala Asp Pro Thr Arg Phe
1          5          10          15

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Phe Thr Asp Asn Leu Leu Ser Pro Glu Asp Trp Gly Leu Gln Asn Ser
          20          25          30

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Thr Leu Tyr Ser Gly Leu Asp Glu Val Ala Glu Glu Gln Thr Gln Leu
          35          40          45

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Phe Arg Cys Pro Glu Gln Asp Val Pro Phe Asp Gly Ser Ser Leu Asp

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50

55 .

60

Val Gly Met Asp Val Ser Pro Ser Glu Pro Pro Trp Glu Leu Leu Pro  
65 70 75 80

Ile Phe Pro Asp Leu Gln Val Lys Ser Glu Pro Ser Ser Pro Cys Ser  
85 90 95

Ser Ser Ser Leu Ser Ser Glu Ser Ser Arg Leu Ser Thr Glu Pro Ser  
100 105 110

Ser Glu Ala Leu Gly Val Gly Glu Val Leu His Val Lys Thr Glu Ser  
115 120 125

Leu Ala Pro Pro Leu Cys Leu Leu Gly Asp Asp Pro Thr Ser Ser Phe  
130 135 140

Glu Thr Val Gln Ile Asn Val Ile Pro Thr Ser Asp Asp Ser Ser Asp  
145 150 155 160

Val Gln Thr Lys Ile Glu Pro Val Ser Pro Cys Ser Ser Val Asn Ser  
165 170 175

Glu Ala Ser Leu Leu Ser Ala Asp Ser Ser Ser Gln Ala Phe Ile Gly  
180 185 190

Glu Glu Val Leu Glu Val Lys Thr Glu Ser Leu Ser Pro Ser Gly Cys  
195 200 205

Leu Leu Trp Asp Val Pro Ala Pro Ser Leu Gly Ala Val Gln Ile Ser  
210 215 220

Met Gly Pro Ser Leu Asp Gly Ser Ser Gly Lys Ala Leu Pro Thr Arg  
225 230 235 240

Lys Pro Pro Leu Gln Pro Lys Pro Val Val Leu Thr Thr Val Pro Met  
245 250 255

Pro Ser Arg Ala Val Pro Pro Ser Thr Thr Val Leu Leu Gln Ser Leu  
260 265 270

Val Gln Pro Pro Pro Val Ser Pro Val Val Leu Ile Gln Gly Ala Ile  
275 280 285

Arg Val Gln Pro Glu Gly Pro Ala Pro Ser Leu Pro Arg Pro Glu Arg  
290 295 300



Lys Ser Ile Val Pro Ala Pro Met Pro Gly Asn Ser Cys Pro Pro Glu  
 305 310 315 320

Val Asp Ala Lys Leu Leu Lys Arg Gln Gln Arg Met Ile Lys Asn Arg  
 325 330 335

Glu Ser Ala Cys Gln Ser Arg Arg Lys Lys Lys Glu Tyr Leu Gln Gly  
 340 345 350

Leu Glu Ala Arg Leu Gln Ala Val Leu Ala Asp Asn Gln Gln Leu Arg  
 355 360 365

Arg Glu Asn Ala Ala Leu Arg Arg Arg Leu Glu Ala Leu Leu Ala Glu  
 370 375 380

Asn Ser Glu Leu Lys Leu Gly Ser Gly Asn Arg Lys Val Val Cys Ile  
 385 390 395 400

Met Val Phe Leu Leu Phe Ile Ala Phe Asn Phe Gly Pro Val Ser Ile  
 405 410 415

Ser Glu Pro Pro Ser Ala Pro Ile Ser Pro Arg Met Asn Lys Gly Glu  
 420 425 430

Pro Gln Pro Arg Arg His Leu Leu Gly Phe Ser Glu Gln Glu Pro Val  
 435 440 445

Gln Gly Val Glu Pro Leu Gln Gly Ser Ser Gln Gly Pro Lys Glu Pro  
 450 455 460

Gln Pro Ser Pro Thr Asp Gln Pro Ser Phe Ser Asn Leu Thr Ala Phe  
 465 470 475 480

Pro Gly Gly Ala Lys Glu Leu Leu Leu Arg Asp Leu Asp Gln Leu Phe  
 485 490 495

Leu Ser Ser Asp Cys Arg His Phe Asn Arg Thr Glu Ser Leu Arg Leu  
 500 505 510

Ala Asp Glu Leu Ser Gly Trp Val Gln Arg His Gln Arg Gly Arg Arg  
 515 520 525

Lys Ile Pro Gln Arg Ala Gln Glu Arg Gln Lys Ser Gln Pro Arg Lys  
 530 535 540

Lys Ser Pro Pro Val Lys Ala Val Pro Ile Gln Pro Pro Gly Pro Pro  
 545 550 555 560

Glu Arg Asp Ser Val Gly Gln Leu Gln Leu Tyr Arg His Pro Asp Arg  
565 570 575

Ser Gln Pro Ala Phe Leu Asp Ala Ile Asp Arg Arg Glu Asp Thr Phe  
580 585 590

Tyr Val Val Ser Phe Arg Arg Asp His Leu Leu Leu Pro Ala Ile Ser  
595 600 605

His Asn Lys Thr Ser Arg Pro Lys Met Ser Leu Val Met Pro Ala Met  
610 615 620

Ala Pro Asn Glu Thr Leu Ser Gly Arg Gly Ala Pro Gly Asp Tyr Glu  
625 630 635 640

Glu Met Met Gln Ile Glu Cys Glu Val Met Asp Thr Arg Val Ile His  
645 650 655

Ile Lys Thr Ser Thr Val Pro Pro Ser Leu Arg Lys Gln Pro Ser Pro  
660 665 670

Thr Pro Gly Asn Ala Thr Gly Gly Pro Leu Pro Val Ser Ala Ala Ser  
675 680 685

Gln Ala His Gln Ala Ser His Gln Pro Leu Tyr Leu Asn His Pro  
690 695 700

<210> 19  
<211> 2013  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<223> DNA that codes for ATF6

<400> 19  
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actgatgagc tgcaattgga agcagcaaat gagacgtatg aaaacaattt tgataatctt 180  
gattttgatt tggatttgat gcottgggag tcagacattt gggacatcaa caaccaaadc 240  
tgtacagtta aagatattaa ggcagaacct cagccacttt ctccagcctc ctcaagttat 300  
tcagtctcgt ctctcgggc agtggactct tattcttcaa ctacagcatgt tcttgaggag 360  
ttggatttgt cttctagttc tcagatgtct cccctttcct tatatggtga aaactctaata 420  
agtctctctt cagcgggagc actgaaggaa gataagcctg tcaactggtcc taggaacaag 480

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actgaaaatg gactgactcc aaagaaaaaa attcaggtga attcaaaacc ttcaattcag      540
cccaagcctt tattgcttcc agcagcaccc aagactcaaa caaactccag tgttccagca      600
aaaaccatca ttattcagac agtaccaacg cttatgccat tggcaaagca gcaaccaatt      660
atcagttttac aacctgcacc cactaaaggc cagacggttt tgctgtctca gcctactgtg      720
gtacaacttc aagcacctgg agttctgccc tctgctcagc cagtccttgc tgttgctggg      780
ggagtcacac agctccctaa tcacgtggtg aatgtggtac cagccccttc agcgaatagc      840
ccagtgaatg gaaaactttc cgtgactaaa cctgtcctac aaagtacat gagaaatgtc      900
ggttcagata ttgctgtgct aaggagacag caacgtatga taaaaaatcg agaatccgct      960
tgtcagtctc gcaagaagaa gaaagaatat atgctagggt tagaggcgag attaaaggct    1020
gccctctcag aaaacgagca actgaagaaa gaaaatggaa cactgaagcg gcagctggat    1080
gaagttgtgt cagagaacca gaggcttaaa gtccctagtc caaagcgaag agttgtctgt    1140
gtgatgatag tattggcatt tataatactg aactatggac ctatgagcat gttggaacag    1200
gattccagga gaatgaaccc tagtgtgagc cctgcaaatc aaaggaggca ctttctagga    1260
ttttctgcta aagaggcaca ggacacatca gatggtatta tccagaaaaa cagctacaga    1320
tatgatcatt ctgtttcaaa tgacaaagcc ctgatggtgc taactgaaga accattgctt    1380
tacattcctc cacctccttg tcagccccta attaacacaa cagagtctct caggttaaat    1440
catgaacttc gaggatgggt tcatagacat gaagtagaaa ggaccaagtc aagaagaatg    1500
acaataatc aacagaaaac ccgtattctt caggggtgctc tggaacaggg ctcaaattct    1560
cagctgatgg ctgttcaata cacagaaacc actagtagta tcagcaggaa ctcagggagt    1620
gagctacaag tgtattatgc ttcacccaga agttatcaag acttttttga agccatccgc    1680
agaaggggag acacatttta tgttgtgtca tttogaaggg atcacctgct gttaccagct    1740
accacccata acaagaccac aagacaaaaa atgtcaattg tgttaccagc aataaacata    1800
aatgagaatg tgatcaatgg gcaggactac gaagtgatga tgcagattga ctgtcagggtg    1860
atggacacca ggatcctcca tatcaaaagt tcgtcagttc ctccttacct ccgagatcag    1920
cagaggaatc aaaccaacac cttctttggc tcccctcccg cagccacaga ggcaaccac     1980
gttgtcagca ccatccctga gtcattacaa tag                                2013

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<210> 20
<211> 670
<212> PRT
<213> Homo sapiens

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<220>
<221> misc_feature
<223> ATF6

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<400> 20

Met Gly Glu Pro Ala Gly Val Ala Gly Thr Met Glu Ser Pro Phe Ser  
1 5 10 15

Pro Gly Leu Phe His Arg Leu Asp Glu Asp Trp Asp Ser Ala Leu Phe  
20 25 30

Ala Glu Leu Gly Tyr Phe Thr Asp Thr Asp Glu Leu Gln Leu Glu Ala  
35 40 45

Ala Asn Glu Thr Tyr Glu Asn Asn Phe Asp Asn Leu Asp Phe Asp Leu  
50 55 60

Asp Leu Met Pro Trp Glu Ser Asp Ile Trp Asp Ile Asn Asn Gln Ile  
65 70 75 80

Cys Thr Val Lys Asp Ile Lys Ala Glu Pro Gln Pro Leu Ser Pro Ala  
85 90 95

Ser Ser Ser Tyr Ser Val Ser Ser Pro Arg Ser Val Asp Ser Tyr Ser  
100 105 110

Ser Thr Gln His Val Pro Glu Glu Leu Asp Leu Ser Ser Ser Gln  
115 120 125

Met Ser Pro Leu Ser Leu Tyr Gly Glu Asn Ser Asn Ser Leu Ser Ser  
130 135 140

Ala Glu Pro Leu Lys Glu Asp Lys Pro Val Thr Gly Pro Arg Asn Lys  
145 150 155 160

Thr Glu Asn Gly Leu Thr Pro Lys Lys Lys Ile Gln Val Asn Ser Lys  
165 170 175

Pro Ser Ile Gln Pro Lys Pro Leu Leu Leu Pro Ala Ala Pro Lys Thr  
180 185 190

Gln Thr Asn Ser Ser Val Pro Ala Lys Thr Ile Ile Ile Gln Thr Val  
195 200 205

Pro Thr Leu Met Pro Leu Ala Lys Gln Gln Pro Ile Ile Ser Leu Gln  
210 215 220

Pro Ala Pro Thr Lys Gly Gln Thr Val Leu Leu Ser Gln Pro Thr Val  
225 230 235 240

Val Gln Leu Gln Ala Pro Gly Val Leu Pro Ser Ala Gln Pro Val Leu  
245 250 255

Ala Val Ala Gly Gly Val Thr Gln Leu Pro Asn His Val Val Asn Val  
260 265 270

Val Pro Ala Pro Ser Ala Asn Ser Pro Val Asn Gly Lys Leu Ser Val  
275 280 285

Thr Lys Pro Val Leu Gln Ser Thr Met Arg Asn Val Gly Ser Asp Ile  
290 295 300

Ala Val Leu Arg Arg Gln Gln Arg Met Ile Lys Asn Arg Glu Ser Ala  
305 310 315 320

Cys Gln Ser Arg Lys Lys Lys Lys Glu Tyr Met Leu Gly Leu Glu Ala  
325 330 335

Arg Leu Lys Ala Ala Leu Ser Glu Asn Glu Gln Leu Lys Lys Glu Asn  
340 345 350

Gly Thr Leu Lys Arg Gln Leu Asp Glu Val Val Ser Glu Asn Gln Arg  
355 360 365

Leu Lys Val Pro Ser Pro Lys Arg Arg Val Val Cys Val Met Ile Val  
370 375 380

Leu Ala Phe Ile Ile Leu Asn Tyr Gly Pro Met Ser Met Leu Glu Gln  
385 390 395 400

Asp Ser Arg Arg Met Asn Pro Ser Val Ser Pro Ala Asn Gln Arg Arg  
405 410 415

His Leu Leu Gly Phe Ser Ala Lys Glu Ala Gln Asp Thr Ser Asp Gly  
420 425 430

Ile Ile Gln Lys Asn Ser Tyr Arg Tyr Asp His Ser Val Ser Asn Asp  
435 440 445

Lys Ala Leu Met Val Leu Thr Glu Glu Pro Leu Leu Tyr Ile Pro Pro  
450 455 460

Pro Pro Cys Gln Pro Leu Ile Asn Thr Thr Glu Ser Leu Arg Leu Asn  
465 470 475 480

His Glu Leu Arg Gly Trp Val His Arg His Glu Val Glu Arg Thr Lys  
485 490 495

Ser Arg Arg Met Thr Asn Asn Gln Gln Lys Thr Arg Ile Leu Gln Gly  
500 505 510

Ala Leu Glu Gln Gly Ser Asn Ser Gln Leu Met Ala Val Gln Tyr Thr  
515 520 525

Glu Thr Thr Ser Ser Ile Ser Arg Asn Ser Gly Ser Glu Leu Gln Val  
530 535 540

Tyr Tyr Ala Ser Pro Arg Ser Tyr Gln Asp Phe Phe Glu Ala Ile Arg  
545 550 555 560

Arg Arg Gly Asp Thr Phe Tyr Val Val Ser Phe Arg Arg Asp His Leu  
565 570 575

Leu Leu Pro Ala Thr Thr His Asn Lys Thr Thr Arg Pro Lys Met Ser  
580 585 590

Ile Val Leu Pro Ala Ile Asn Ile Asn Glu Asn Val Ile Asn Gly Gln  
595 600 605

Asp Tyr Glu Val Met Met Gln Ile Asp Cys Gln Val Met Asp Thr Arg  
610 615 620

Ile Leu His Ile Lys Ser Ser Ser Val Pro Pro Tyr Leu Arg Asp Gln  
625 630 635 640

Gln Arg Asn Gln Thr Asn Thr Phe Phe Gly Ser Pro Pro Ala Ala Thr  
645 650 655

Glu Ala Thr His Val Val Ser Thr Ile Pro Glu Ser Leu Gln  
660 665 670

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<211> 36  
<212> DNA  
<213> Artificial

<220>  
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for use as a primer to obtain mature HtrA2 DNA

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36

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<212> DNA  
<213> Artificial

<220>  
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 for use as a primer to obtain mature HtrA2 DNA

<400> 22  
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<210> 23  
 <211> 40  
 <212> DNA  
 <213> Artificial

<220>  
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 for use as a primer to obtain mature HtrA2(S306A) DNA

<400> 23  
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<210> 24  
 <211> 40  
 <212> DNA  
 <213> Artificial

<220>  
 <223> Designed polynucleotide based on the base sequence of SEQ ID NO:3  
 for use as a primer to obtain mature HtrA2(S306A) DNA

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<210> 26  
 <211> 37  
 <212> DNA  
 <213> Artificial

<220>  
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<210> 27  
 <211> 27  
 <212> DNA

<213> Artificial

<220>

<223> Designed polynucleotide based on the base sequence of SEQ ID NO:1  
7 for use as a primer to obtain CREBL1 DNA

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gcgaattcgc catggcggag ctgatgc 27

<210> 28  
<211> 28  
<212> DNA  
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<220>

<223> Designed polynucleotide based on the base sequence of SEQ ID NO:1  
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<210> 29  
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<212> DNA  
<213> Artificial

<220>

<223> Designed polynucleotide based on the base sequence of SEQ ID NO:1  
7 for use as a primer to obtain CREBL1 DNA

<400> 29  
gcggatcccg cggagctgat gctgctcagc 30

<210> 30  
<211> 33  
<212> DNA  
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cctcgagggt taggatgat tgaggtagag ggg 33

<210> 31  
<211> 30  
<212> DNA  
<213> Artificial

<220>

<223> Designed polynucleotide based on the base sequence of SEQ ID NO:1  
9 for use as a primer to obtain ATF6 DNA

<400> 31  
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<210> 32



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 for use as a primer to obtain mature HtrA2(delta AVPS) DNA  
  
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36